

In The Claims

Please amend the claims as follows:

Sub 1
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1. (Amended) Method to detect and phenotype target cells[, such as animal and human cells,] in cell suspensions by using particles coated with antibodies directed against antigenic determinants/receptors expressed on the target cells, except when the target cells are malignant and normal haematopoietic and lymphatic cells, [characterized in that] wherein 2 [-] to 6 antibodies [, each antibody conjugated to each of several types of particles instrumentally or visually separable by fluorescence, color and size, with sizes ranging from 0.01µm - 6µm, wherein the ratio between the number of particles and the number of cells ranges from 20 : 1 to 0.5 : 1,] are incubated under gentle rotation for about 5[-10] minutes to about 2 hours with cell suspensions containing the target cells at 0°C to 25°C, optionally followed by [a per se known] an enrichment procedure, and evaluation of the target cell rosettes microscopically and/or by suitable visualizing or imaging devices, and wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01µm - 6µm, each antibody of the 2 - 6 antibodies is conjugated to different particles, and the ratio between the number of particles and the number of cells ranges from 0.5 : 1 to 20 : 1.

Sub 2
2. (Amended) Method according to claim 1, [characterized in that] wherein the said size of the particles ranges from about 0.5µm [-] to about 4.5µm, the said ratio is 5 : 1 (number of particles/number of cells), the said incubation time is 30 minutes and the said incubation temperature is 4 °C

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3. (Amended) Method according to claim 1, [characterized in that] wherein the particles used in the method are separable by a combination of fluorescence and/or size or a combination of fluorescent emission spectra, different colors or different sizes.

4. (Amended) Method according to claim 3, [characterized in that] wherein the particles used are separable by a combination of fluorescent emission spectra and/or size.

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5. (Amended) Method according to claim 7, [characterized in that] wherein the particles used in the method are coated with antibodies directed against the receptors/antigens [listed in Table 1] selected from the group consisting of integrins, ICAM-1 (CD54), VCAM-1, NCAM (CD56), HCAM, LCAM, CD44, CD44 variants, ELAM-1, E-selectin, P-selectin, LFA (CD58), MACAN-1, E-cadherin, P-cadherin, tenascin, thrombospondin receptor (CD36), VLA-2, T-antigen, Tn-antigen, sialyl Tn, galbl-4GlcNac (nL4, 6, 8), gastrointestinal cancer associated antigen, Le^y, di-Le^x, tri Le^x, CA15-

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3 epitope, CEA, lacto-N-fucopentantose III (CD15), GD₃, GD₂, Gb₃, GM₃, GM₂, FucGM₁, EGF receptor, c-erbB-2 (HER2), PDGF α receptor, PDGF β receptor, transferrin receptor, NGF receptor, IL-2 receptor (CD25), c-kit, TNF receptor, high molecular weight melanoma antigen (HMW 250,000), Mw105 melanoma-associated glycoprotein, 100 kDa antigen (melanoma/carcinoma), gp 113, p95-100, gp75/TRP-1, gp 100-107, MAA, M125kD (gp125), MAGE 1, MAGE 2, MAGE 3, tyrosinase, TP-1 epitope, Tp-3 epitope, M.200kD sarcoma antigen, M.160kD sarcoma antigen, EGP-2 (cluster 2 epithelial antigen), MUC-1 antigens, MUC-2, MUC-3, LUBCRU-G7 epitope (gp 230kD), prostate specific antigen, prostate cancer antigen, prostate high molecular antigen (M.>400kD), polymorphic epithelial mucins, prostate specific membrane antigen (Cyt-356), human milk fat globin, 42kD breast carcinoma epitope, Mw > 10⁶ mucin, ovarian carcinoma OC125 epitope (m. 750 kD), pancreatic HMW glycoprotein, colon antigen Co-17-1A (M. 37000), Ga 733.2, TAG 72, pancreatic cancer associated marker, pancarcinoma marker, prostrate adenocarcinoma-antigen, Mw 150-130kD adenocarcinoma marker, Mw 92kD bladder carcinoma marker, Mw 600kD bladder carcinoma marker, bladder carcinoma antigen, hepatocellular carcinoma antigen, Mw 48kD colorectal carcinoma marker, colon specific antigen, lung carcinoma antigen M. 350-420kD, colon cancer-associated marker, bladder carcinoma antigens, neuroblastoma-associated epitope, Mel-14 epitope, HMW 250kD glioma antigen, M. 18-22kD head and neck cancer antigen, HLA Class 1 antigen, HLA-A, HLA-B, HLA-A2, HLA-ABC, HLA-DR, HLA-DQ, HLA-DP, β 2-microglobulin, Fas (CD95/APO-1), FAsL, P75, cathepsin D, neuroglandular antigen (CD63), pan-human cell antigen, motility related antigens, proliferation-associated markers, differentiation-associated markers, drug resistance-related markers, angiogenesis-associated markers, chemokine receptor markers, invasion-related antigens, B-cell CD antigens, and T-cell CD antigens.

7. (Amended) Method according to claims 1, [characterized in that] wherein the particles used in the method are coated with antibodies directed to tumor associated antigens.

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8. (Amended) Method according to claim 7, [characterized in that] wherein the tumor associated antigens are MOC31 anti EGP2 (anti-epithelial cell marker) antibody, anti-breast mucin (MUC1) antibody (BM7), 595, anti-EGF receptor (425.3), anti-erbB2 and anti-HMW melanoma antigen (9.2.27).

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9. (Amended) [Use of the method] Method according to claim 1, wherein [it is performed] phenotyping of the target cells is performed, the phenotyping comprising profiling the antigenic determinants or receptors expressed on the cell membrane of the target cells.

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10. (Amended) [Use] Method according to claim 9, wherein the target cell characteristics of biologically informative markers of diagnostic, prognostic and therapeutic value are registered.

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11. (Amended) [Use] Method according to claim 10, wherein the target cells are malignant cells.

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12. (Amended) [Use] Method according to claim 10, wherein the biologically informative markers are adhesion molecules, growth factor receptors, carcinoma markers, carbohydrate antigens, melanoma antigens, sarcoma antigens, glioma antigens, apoptosis associated markers, motility related markers, proliferation associated antigens, differentiation associated markers, drug resistance markers, angiogenesis associated markers, chemokine receptors, invasion-related markers and other antigens.

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13. (Amended) [Use] Method according to claim 1, wherein the biologically informative markers [adhesion molecules] are E-cadherin, [the growth factor receptors are] EGFr, c-erbB2, IL-2 receptor, TNF receptor, [the carcinoma markers are] EGP2, MUC1, MUC2 & 3, PSA, PSM, GA733.2, TAG72, 15-3 epitope, ovarian carcinoma CA-125 epitope, [the carbohydrate antigens are] Le^y, CEA, 15-3 epitope, [the melanoma antigens are] HMW 250000 melanoma antigen, gp75/TRP-1, p95, MAG 1, MAG 2, MAG 3, [the sarcoma antigens are] TP 1 and TP 3 epitopes, [the glioma antigens such as] Mel-14 epitope, [apoptosis associated markers are] Fas, FasL, p75, [the motility related markers are] KAT-1, AMF, [the proliferation associated antigens are] gp120, [the differentiation associated markers are] MUC 18, TA99, [the drug resistance markers are] MDR, MRP, [the angiogenesis associated antigens are] VEGFr, bFGF, [the chemokine receptors are] CCR, CXCR, [the invasion-related markers are] uPAR, uPA, PAI-1, TIMP1 & 2, MMP9, stromelysins, and [the other antigens are] cathepsin D and par-human epitope.

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14. (Amended) Kit [to perform the method] to detect and phenotype target cells, such as animal and human cells, in cell suspensions by using particles coated with antibodies/ligands directed against antigenic determinants/receptors expressed on the target cells, except when the target cells are malignant and normal haematopoietic and lymphatic cells, [characterized in that] wherein 2 - 6 antibodies or ligands, [each antibody or ligand conjugated to each of several types of particles instrumentally or visually separable by fluorescence, color and size, with sizes ranging from 0.01 μ m - 6 μ m, wherein the ratio between the number of particles and the number of cells ranges from 20 : 1 to 0.5 : 1,] are incubated under gentle rotation for 5-10 minutes to 2 hours with cell suspensions containing the target cells at [00C to 250C] 0°C to 25°C, optionally followed by [a per se known] an enrichment procedure, and evaluation of the target cell rosettes

microscopically and/or by suitable visualizing or imaging devices, [characterized in that it] wherein the kit comprises particles conjugated to antibodies/ligands [according to claim 5], wherein one antibody is conjugated to one type of particle instrumentally or visually separable by fluorescence, color and size, with sizes of the particles ranging from 0.01 μ m - 6 μ m, each antibody of the 2 - 6 antibodies is conjugated to the same or different particles, and the ratio between the number of particles and the number of cells ranges from 0.5 : 1 to 20 : 1.

15. (New) Method according to claim 1, wherein the target cells are animal cells or human cells.

16. (New) Kit according to claim 14, wherein the target cells are animal cells or human cells.

REMARKS

Applicant thanks the Examiner for the care and time taken in consideration of the above-referenced patent application and claims.

No new matter has been added. Claims 1-4, 7-11, and 13-14 have been amended to make the claims more clear and definite; new claims 15 and 16, which incorporate deleted language from claims 1 and 14, respectively, have been added; and the specification has been amended to correct typographical errors.

Objections

Claim 14 was objected to because of typographical errors, which have been corrected with the above claim amendments. Claim 1 was objected to for reciting ranges in an order that the Examiner deemed obscure and complex. The claim has been amended to recite the range from smallest to largest. Claim 14 has been similarly amended. Withdrawal of the objections is respectfully requested.